

What is Claimed Is:

1. A process for preparing a mixture of a 5,7,3',4'-tetra-*O*-protected epicatechin (4 β ,8)-
dimer and other oligomers comprises the step of coupling a 5,7,3',4'-tetra-*O*-protected
5 epicatechin monomer with a 5,7,3',4'-tetra-*O*-protected-4-acyloxy epicatechin monomer in the
presence of an acidic clay.
2. A process for preparing a mixture of 5,7,3',4'-tetra-*O*-protected epicatechin (4 β ,8)-
oligomers comprises the step of coupling a 5,7,3',4'-tetra-*O*-protected epicatechin (4 β ,8)-
oligomer with a 5,7,3',4'-tetra-*O*-protected-4-acyloxy epicatechin monomer in the presence of an
10 acidic clay.
3. The process of Claim 1 or 2, wherein the acidic clay is a montmorillonite clay.
4. The process of Claim 1, wherein the protecting groups on the protected monomers are
protecting groups which do not deactivate the A ring of the protected monomers.
5. The process of Claim 2, wherein the protecting groups on the protected oligomer are
15 protecting groups that do not deactivate the A ring of the upper mer of the oligomer and the
protecting groups on the protected monomer are protecting groups that do not deactivate that A
ring of the monomer.
6. The process of Claim 4 or 5, wherein the protecting groups are benzyl groups.
7. The process of Claim 1 or 2, wherein the 4-acyloxy group is a C₂-C₆ alkoxy group having
20 a terminal hydroxyl group.
8. The process of Claim 7, wherein the C₂-C₆ alkoxy group having the terminal hydroxyl
group is a 2-hydroxyethoxy group.

9. The process of Claim 1, wherein the protected monomers are 5,7,3',4'-tetra-*O*-benzylepicatechin and 5,7,3',4'-tetra-*O*-benzyl-4-[2-hydroxyethoxy]epicatechin; wherein the mixture comprises the benzyl-protected epicatechin (4 β ,8)-dimer and benzyl-protected epicatechin (4 β ,8)₂-trimer.
- 5 10. The process of Claim 9, wherein the benzyl-protected epicatechin (4 β ,8)-dimer is the major product in the mixture.
11. The process of Claim 2, wherein the oligomer is a benzyl-protected (4 β ,8)-dimer; wherein the monomer is 5,7,3',4'-tetra-*O*-benzyl-4-[2-hydroxyethoxy]epicatechin; and wherein the mixture comprises a benzyl-protected epicatechin (4 β ,8) -dimer, a (4 β ,8)₂-trimer, and a
- 10 (4 β ,8)₃-tetramer.
12. The process of Claim 1, further comprising the step of separating the protected dimer and other protected oligomers from the monomer by column chromatography.
13. The process of Claim 2, further comprising the step of separating the protected oligomers and protected monomer by column chromatography.
- 15 14. The process of Claim 12 or 13, further comprising the step of replacing the protecting groups on the separated dimer or oligomers with hydrogen.
15. A process for preparing a mixture of benzyl-protected (4 β , 8)-oligomers of epicatechin or catechin comprises reacting a 5,7,3',4'-tetra-*O*-benzyl-protected epicatechin or catechin monomer or a 5,7,3',4'-tetra-*O*-benzyl-protected (4 β ,8)-epicatechin or catechin oligomer and 3-*O*-acetyl-4-
- 20 [(2-benzothiazolyl)thio]-5,7,3',4'-tetra-*O*-benzylepicatechin in the presence of silver tetrafluoroborate.

16. A process for preparing a mixture of acetyl-protected and benzyl-protected (4 β ,8)-oligomers of epicatechin or catechin comprises reacting a 3-*O*-acetyl-5,7,3',4'-tetra-*O*-benzylepicatechin monomer or a 3-*O*-acetyl-5,7,3',4'-tetra-*O*-benzylepicatechin (4 β ,8)-oligomer and 3-*O*-acetyl-4-[(2-benzothiazolyl)thio]-5,7,3',4'-tetra-*O*-benzylepicatechin in the presence of
5 silver tetrafluoroborate.
17. The process of Claim 15 or 16, wherein the silver tetrafluoroborate is dried before the reaction.
18. The process of Claim 17, wherein the drying is vacuum drying carried out immediately before the reaction.
- 10 19. The process of Claim 16, wherein the mixture comprises protected trimers through protected octamers.
20. The process of Claim 15 or 16, further comprising the step of isolating the protected oligomers in the mixture by reverse phase high pressure liquid chromatography.
21. The process of Claim 20, further comprising the step of removing the acetyl-protecting
15 group(s) from the isolated oligomers.
22. The process of Claim 21, wherein the acetyl group(s) removal is carried out with aqueous tetra-*n*-butyl ammonium hydroxide.
23. The process of Claim 20, further comprising the step of removing the benzyl-protecting groups from the isolated oligomers.
- 20 24. The process of Claim 23, wherein the benzyl groups removal is carried out by hydrogenolysis.

25. The process of Claim 20, further comprising the steps of removing the acetyl protecting group(s) and then removing the benzyl protecting groups from the isolated oligomers.

26. The process of Claim 25, wherein the acetyl group(s) removal is carried out with aqueous tetra-n-butyl ammonium hydroxide and the benzyl groups removal is carried out by

5 hydrogenolysis.

27. A process for preparing a mixture of 5,7,3',4'-tetra-*O*-benzyl (4 β ,8)-oligomers comprises the steps of:

(a) activating with 2-(benzothiazolyl)thio groups the C-4 positions of each of epicatechin 5,7,3',4'-tetra-*O*-benzylepicatechin; and

10 (b) self condensing the activated, protected monomers in the presence of silver tetrafluoroborate or an acidic clay to form a benzyl-protected condensed epicatechin (4 β ,8)-oligomer.

28. The process of Claim 27, further comprising the steps of separating the protected dimer, trimer, and tetramer removing the benzyl protecting groups.

15 29. A process for chain extending protected epicatechin (4 β ,8)-oligomers comprises the step of condensing an epicatechin (4 β ,8) oligomer having 3-*O*-acetyl protecting groups and 5,7,3',4'-tetra-*O*-benzyl protecting groups on all mers and a C-4-[2(benzothiazolyl)thio] activating group on a terminal mer with an epicatechin oligomer having 3-*O*-acetyl and 5,7,3',4'-tetra-*O*-benzyl protecting groups on each mer in the presence of silver tetrafluoroborate or an acidic clay.

20 30. The process of Claim 29, wherein one of the C-4 activated, protected oligomers is a 3-*O*-acetyl-5,7,3',4'-tetra-*O*-benzylepicatechin-(4 β ,8)-[3-*O*-acetyl-4-[(2-benzothiazolyl)thio]-5,7,3',4'-tetra-*O*-benzylepicatechin]; wherein the benzyl-protected oligomer is tetrakis (3-*O*-acetyl-

5,7,3',4'-tetra-*O*-benzyl)epicatechin (4 β ,8), wherein the protected, chain-extended oligomer is hexakis (3-*O*-acetyl-5,7,3',4'-tetra-*O*-benzyl tetramer epicatechin) (4 β ,8)₅-hexamer.

31. 4-[(2-Benothiazolyl)thio]-5,7,3',4'-tetra-*O*-benzylepicatechin or 4-[(2-benzothiazolyl)thio]- 5,7,3',4'-tetra-*O*-benzylcatechin.

5 32. A process for preparing the compound of Claim 31 comprises reacting 5,7,3',4'-tetra-*O*-benzyl-4-(2-hydroxyethoxy)epicatechin or 5,7,3',4'-tetra-*O*-benzyl-4-(2-hydroxyethoxy)catechin with an organoaluminum thiolate generated from 2-mercaptobenzothiazole.

33. 4-[(2-Benzothiazolyl)thio]-3-*O*-acetyl-5,7,3',4'-tetra-*O*-benzylepicatechin or 4-[(2-benzothiazolyl)thio]-3-*O*-acetyl-5,7,3',4'-tetra-*O*-benzylcatechin.

10 34. A process for preparing the compound of Claim 33 comprises reacting 5,7,3',4'-tetra-*O*-benzyl-4-(2-hydroxyethoxy)epicatechin or 5,7,3',4'-tetra-*O*-benzyl-4-(2-hydroxyethoxy)catechin with an organoaluminum thiolate generated from 2-mercaptobenzothiazole followed by acetylation.

35. A method of treating breast cancer in a mammal in need of such treatment, which
15 treatment inhibits cancer cell growth through cell cycle arrest in the Go/G phase and comprises administering to the mammal epicatechin-(4 β ,8)₄-pentamer, wherein the breast cancer cells are selected from the group consisting of human breast cancer cell lines MCF-7, SKBR-3, MDA 435, and MDA MB-231.

36. The method of Claim 35 wherein the pentamer is a purified procyanidin fraction isolated
20 from cocoa beans as a cocoa extract.

37. The method of Claim 36, wherein the pentamer is a synthetically prepared procyanidin.